

Inter: [REDACTED] Location: [REDACTED]  
PCT/EP 03/50277

519035

IPC 7 G06F19/00 C1201/70

C12N9/50

22 DEC 2004

#### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, SEQUENCE SEARCH

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SCHINAZI ET AL.: "Mutations in retroviral genes associated with drug resistance: 2000-2001 update" INTERNATIONAL ANTIVIRAL NEWS, vol. 8, no. 5, 2000, pages 65-91, XP009018670 the whole document ---	1-20
X	DATABASE NCBI 15 November 2000 (2000-11-15) VERGNE ET AL.: "POL precursor" Database accession no. CAC03089 XP002258544 mutation 41S the whole document ---	15-20

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z document member of the same patent family

Date of the actual completion of the international search

21 October 2003

Date of mailing of the international search report

10/11/2003

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

Intern. Publication No.

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VERGNE LAURENCE ET AL: "Genetic diversity of protease and reverse transcriptase sequences in non-subtype-B human immunodeficiency virus type 1 strains: Evidence of many minor drug resistance mutations in treatment-naive patients" JOURNAL OF CLINICAL MICROBIOLOGY, vol. 38, no. 11, November 2001 (2001-11), pages 3919-3925, XP002258541 ISSN: 0095-1137 mutation 41K and mutation 70E (group 0) page 3923, left-hand column; figure 2 ----	15-20
X	DATABASE NCBI 12 June 2002 (2002-06-12) SCHMIDT ET AL.: "pol protein (HIV-1)" Database accession no. AAK32676 XP002258545 mutation 41T the whole document ----	15-20
X	DATABASE NCBI 23 May 2002 (2002-05-23) ESHLEMAN ET AL.: "HIV1 isolate 420111k042398 from USA pol protein (pol) gene" Database accession no. AF357746 XP002258546 mutation 41I the whole document ----	15-20
P,X	DATABASE SWISSPROT 1 June 2003 (2003-06-01) WATKINS ET AL.: "Protease HIV1" Database accession no. Q7ZCQ9 XP002258547 mutation 41I the whole document ----	15-20
X	RUSCONI STEFANO ET AL: "Susceptibility to PNU-140690 (tipranavir) of human immunodeficiency virus type 1 isolates derived from patients with multidrug resistance to other protease inhibitors" ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 44, no. 5, May 2000 (2000-05), pages 1328-1332, XP002258542 ISSN: 0066-4804 mutation 41K page 1330, left-hand column, paragraph 3 ----	5-8, 11-20
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# INTERNATIONAL SEARCH REPORT

Intern ..... ation No  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE NCBI13 April 2001 (2001-04-13)            SHAFER ET AL.: "HIV-1 isolate PCCPROT48            from USA, protease (pol) gene"            Database accession no. AF085133            XP002258548            mutation 41K            the whole document</p>	15-20
X	<p>DATABASE SWISSPROT            1 July 1997 (1997-07-01)            CONDRA ET AL.: "HIV-1 protease"            Database accession no. 010176            XP002258549            Mutation 41K            the whole document</p>	15-20
X	<p>CONDRA J ET AL: "Genetic correlation of            in vivo viral isolates to indinavir, a            human immunodeficiency type 1 protease            inhibitor"            JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY            FOR MICROBIOLOGY, US,            vol. 70, no. 12, December 1996 (1996-12),            pages 8270-76, XP002150116            ISSN: 0022-538X            mutation 41K            table 1</p>	5-8, 11-20
X	<p>HERTOGS ET AL: "A Rapid Method for            Simultaneous Detection of Phenotypic            Resistance to Inhibitors of Protease and            Reverse Transcriptase in Recombinant Human            Immunodeficiency Virus Type 1 Isolates            from Patients Treated with Antiretroviral            Drugs"            ANTIMICROBIAL AGENTS AND CHEMOTHERAPY,            AMERICAN SOCIETY FOR MICROBIOLOGY,            WASHINGTON, DC, US,            vol. 42, no. 2, February 1998 (1998-02),            pages 269-276, XP002137814            ISSN: 0066-4804            mutation 41K            table 6</p>	1-20

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## INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VASUDEVACHARI M B ET AL: "EMERGENCE OF PROTEASE INHIBITOR RESISTANCE MUTATIONS IN HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 ISOLATES FROM PATIENTS AND RAPID SCREENING PROCEDURE FOR THEIR DETECTION" ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, DC, US, vol. 40, no. 11, November 1996 (1996-11), pages 2535-2541, XP000901688 ISSN: 0066-4804 mutation 41K figure 4	15-20
X	--- DATABASE NCBI12 June 2002 (2002-06-12) SCHMIDT ET AL.: "HIV-1 isolate 992286 from Germany pol protein (pol) gene" Database accession no. AF347471 XP002258550 mutation 41Q the whole document	15-20
X	--- DATABASE NCBI30 August 2000 (2000-08-30) ABREMSKI ET AL.: "pol protein HIV-1" Database accession no. AAG03320 XP002258551 mutation 41G the whole document	15-20
X	--- DATABASE NCBI16 August 2001 (2001-08-16) GONZALES ET AL.: "pol polyprotein (HIV-1)" Database accession no. AAK35843 XP002258552 mutation 70E the whole document	15-20
X	--- DATABASE NCBI3 February 2000 (2000-02-03) MARTINEZ ET AL.: "protease (HIV-1)" Database accession no. AAF29689 XP002258553 mutation 70E the whole document	15-20
X	--- IBÁÑEZ A ET AL: "Human immunodeficiency virus type 1 population bottleneck during indinavir therapy causes a genetic drift in the env quasispecies." THE JOURNAL OF GENERAL VIROLOGY. ENGLAND JAN 2000, vol. 81, no. Pt 1, January 2000 (2000-01), pages 85-95, XP002258543 ISSN: 0022-1317 mutations 41K and 70E figure 2A	1-20
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# INTERNATIONAL SEARCH REPORT

Inter ... 1 Application No  
PCT/EP 03/50277

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01 79540 A (DEHERTOGH PASCALE ALFONS ROSA ;HERTOGS KURT (BE); VIRCO NV (BE); M) 25 October 2001 (2001-10-25) the whole document ----	1-20
A	WO 02 22076 A (VIROLOGIC INC) 21 March 2002 (2002-03-21) the whole document ----	1-20
A	WO 99 67428 A (INNOGENETICS NV ;STUYVER LIEVEN (BE)) 29 December 1999 (1999-12-29) the whole document -----	1-20

# INTERNATIONAL SEARCH REPORT

International application No.  
- PCT/EP 03/50277

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1,3,5,7,9,11,13,15,17,19 (partially)

A computer system correlating the presence of the mutation 41S in HIV-1 protease with a change in susceptibility to a protease inhibitor, methods of evaluating the effectiveness of a protease inhibitor against said protease mutant and of identifying drugs effective against said protease mutant, a vector comprising an HIV sequence having said mutation, an isolated HIV protease having said mutation and an oligonucleotide comprising an HIV protease sequence having said mutation.

2. Claims: 1-20 (partially)

A computer system correlating the presence of the mutation 41T in HIV-1 protease with a change in susceptibility to a protease inhibitor, methods of evaluating the effectiveness of a protease inhibitor against said protease mutant and of identifying drugs effective against said protease mutant, a vector comprising an HIV sequence having said mutation, an isolated HIV protease having said mutation and an oligonucleotide comprising an HIV protease sequence having said mutation.

3. Claims: 1-20 (partially)

A computer system correlating the presence of the mutation 41I in HIV-1 protease with a change in susceptibility to a protease inhibitor, methods of evaluating the effectiveness of a protease inhibitor against said protease mutant and of identifying drugs effective against said protease mutant, a vector comprising an HIV sequence having said mutation, an isolated HIV protease having said mutation and an oligonucleotide comprising an HIV protease sequence having said mutation.

4. Claims: 1-20 (partially)

A computer system correlating the presence of the mutation 41K in HIV-1 protease with a change in susceptibility to a protease inhibitor, methods of evaluating the effectiveness of a protease inhibitor against said protease mutant and of identifying drugs effective against said protease mutant, a vector comprising an HIV sequence having said mutation, an isolated HIV protease having said mutation and an oligonucleotide comprising an HIV protease sequence having said mutation.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

5. Claims: 1-20 (partially)

A computer system correlating the presence of the mutation 41G in HIV-1 protease with a change in susceptibility to a protease inhibitor, methods of evaluating the effectiveness of a protease inhibitor against said protease mutant and of identifying drugs effective against said protease mutant, a vector comprising an HIV sequence having said mutation, an isolated HIV protease having said mutation and an oligonucleotide comprising an HIV protease sequence having said mutation.

6. Claims: 1-20 (partially)

A computer system correlating the presence of the mutation 70E in HIV-1 protease with a change in susceptibility to a protease inhibitor, methods of evaluating the effectiveness of a protease inhibitor against said protease mutant and of identifying drugs effective against said protease mutant, a vector comprising an HIV sequence having said mutation, an isolated HIV protease having said mutation and an oligonucleotide comprising an HIV protease sequence having said mutation.



# INTERNATIONAL SEARCH REPORT

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Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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			EP 1332231 A2	06-08-2003
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			US 2002064838 A1	30-05-2002
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			AU 4900199 A	10-01-2000
			BR 9911395 A	06-11-2001
			CA 2330234 A1	29-12-1999
			WO 9967428 A2	29-12-1999
			EP 1090147 A2	11-04-2001
			JP 2002518065 T	25-06-2002